REMARKS

By the above amendment, claims 1 and 30 have been amended, claims 2-27 have been canceled, and claims 32-41 have been added. These amendments do not add prohibited new matter and are fully supported by the specification. Support for these amendments may be found, for example, as indicated in the following listing.

Support for the amendment:

The following page numbers and paragraph numbers were excerpted from United States Patent Application Publication US 2006/0014811 A1.

Claim 1

[Definition of E]

(1) <u>a 2,5- or 3,5-di-substituted phenyl group wherein at least one of said substituent is trifluoromethyl group</u>

Page 2, Paragraph [0015], item (8).

(2) a mono- or di-substituted thiazol-2-yl group

Page 24, Paragraph [0254].

[Definition of the <u>substituents</u> existing in the group described in the aforementioned (1)]

Page 10, Paragraph [0113].

The following explanations are described for the definition of the substituents of the functional group.

"In the present specification, when a certain functional group is defined as "which may be substituted," the definition means that the functional group may sometimes have one or more substituents at chemically substitutable positions, unless otherwise specifically mentioned. Kind of substituents, number of substituents, and the position of substituents existing in the functional groups are not particularly limited, and when two or more substituents exist, they may be the same or different. Examples of the substituent existing in the functional group include, for example, halogen atoms, oxo group, thioxo group, nitro group, nitroso group, cyano group, isocyano group, cyanato group, thiocyanato group, isocyanato group, isothiocyanato group, hydroxy group, sulfanyl group, carboxy group, sulfanylcarbonyl group, oxalo group, methooxalo group, thiocarboxy group, dithiocarboxy group, carbamoyl group, thiocarba moyl group, sulfo group, sulfamoyl group, sulfino group, sulfinamoyl group, sulfeno group, sulfenamoyl group, phosphono group, hydroxyphosphonyl group, hydrocarbon group, heterocyclic group, hydrocarbon-oxy group, heterocyclic ring-oxy group, hydrocarbon-sulfanyl group, heterocyclic ring-sulfanyl group, acyl group, amino group, hydrazino group, hydrazono group, diazenyl group, ureido group, thioureido group, guanidino group, carbamoimidoyl group (amidino group), azido group, imino group, hydroxyamino group, hydroxyimino group, aminooxy group, diazo group, semicarbazino group, semicarbazono group, allophanyl group, hydantoyl group, phosphano group, phosphoroso group, phospho group, boryl group, silyl group, stannyl group, selanyl group, oxido group and the like."

(3) a halogen atom

Page 10, Paragraph [0113].

The "halogen atom" is exemplified as an example of the substituent existing in the functional group.

(4) a nitro group

Page 10, Paragraph [0113].

The "nitro group" is exemplified as an example of the substituent existing in the functional group.

(5) an alkyl group

Page 10, Paragraph [0113].

The "hydrocarbon group" is exemplified as an example of the substituent existing in the functional group.

Page 2, Paragraph [0028].

The "aliphatic hydrocarbon group" is exemplified as an example of the "hydrocarbon group."

Pages 2-3, Paragraph [0029].

The "alkyl group" is exemplified as an example of the "aliphatic hydrocarbon group."

(6) a halogenated alkyl group

Page 10, Paragraph [0115].

The following explanations are described for the definition of the substituents existing in the functional group.

"The above substituents according to the aforementioned definition of "which may be substituted" may further be substituted with the aforementioned substituents at the chemically substitutable positions on the substituent. Kind of substituents, number of substituents, and positions of substituents are not particularly limited, and when the substituents are substituted with two or more substituents, they may be the same or different."

Page 10, Paragraph [0113].

The "hydrocarbon group" is exemplified as an example of the substituent existing in the functional group.

Page 2, Paragraph [0028].

The "aliphatic hydrocarbon group" is exemplified as an example of the "hydroca rbon group."

Pages 2-3, Paragraph [0029].

The "alkyl group" is exemplified as an example of the "aliphatic hydrocarbon group."

Page 10, Paragraph [0113].

The "halogen atom" is exemplified as an example of the substituent existing in the functional group.

(7) an alkoxy group

Page 10, Paragraph [0113].

The "hydrocarbon-oxy group" is exemplified as an example of the substituent existing in the functional group.

Page 5, Paragraph [0059].

The "alkoxy group" is exemplified as an example of the "hydrocarbon-oxy group."

(8) a halogenated alkoxy group

Page 10, Paragraph [0115].

The following explanations are described for the definition of the substituents existing in the functional group.

"The above substituents according to the aforementioned definition of "which may be substituted" may further be substituted with the aforementioned substituents at the chemically substitutable positions on the substituent. Kind of substituents, number of substituents, and positions of substituents are not particularly limited, and when the substituents are substituted with two or more substituents, they may be the same or different."

Page 10, Paragraph [0113].

The "hydrocarbon-oxy group" is exemplified as an example of the substituent existing in the functional group.

Page 5, Paragraph [0059].

The "alkoxy group" is exemplified as an example of the "hydrocarbon-oxy group."

Page 10, Paragraph [0113].

The "halogen atom" is exemplified as an example of the substituent existing in the functional group.

(9) <u>an aryl-oxy group which may be substituted with one or more substituents</u>

Page 10, Paragraph [0113].

The "hydrocarbon-oxy group" is exemplified as an example of the substituent existing in the functional group.

Page 5, Paragraph [0059].

The "aryl-oxy group" is exemplified as an example of the "hydrocarbon-oxy group."

(10) a halogen atom (existing in the aforementioned "aryl-oxy group")

According to the aforementioned (3), the "alkoxy group" is thought to be an example of the substituent existing in the functional group.

(11) an alkoxy group (existing in the aforementioned "aryl-oxy group")

According to the aforementioned (7), the "alkoxy group" is thought to be an example of the substituent existing in the functional group.

(12) an alkyl group (existing in the aforementioned "aryl-oxy group")

According to the aforementioned (5), the "alkyl group" is thought to be an example of the substituent existing in the functional group.

(13) <u>a cyano group (existing in the aforementioned "aryl-oxy group")</u> Page 10, Paragraph [0113].

The "cyano group" is exemplified as an example of the substituent existing in the functional group.

(14) an alkyl-sulfanyl group

Page 10, Paragraph [0113].

The "hydrocarbon-sulfanyl group" is exemplified as an example of the substituent existing in the functional group.

Page 6, Paragraph [0074].

The "alkyl-sulfanyl group" is exemplified as an example of the "hydrocarbon-sulfanyl group."

(15) an alkoxy-carbonyl group

Page 10, Paragraph [0113].

The "acyl group" is exemplified as an example of the substituent existing in the functional group.

Pages 7-8, Paragraph [0088].

The group represented by the formula $(\omega\text{-}2A)$ is exemplified as an example of the "acyl group."

Page 9, Paragraph [0090].

The "hydrocarbon-oxy-carbonyl group" is exemplified as an example of the group represented by the formula $(\omega-2A)$.

Page 5, Paragraph [0059].

The "alkoxy group" is exemplified as an example of the "hydrocarbon-oxy group."

(16) a carboxy group

Page 10, Paragraph [0113].

The "carboxy group" is exemplified as an example of the substituent existing in the functional group.

(17) <u>a monocyclic non-aromatic heterocyclic group which may be substituted with one or more halogenated alkyl groups</u>

Page 10, Paragraph [0113].

The "heterocyclic group" is exemplified as an example of the substituent existing in the functional group.

Page 4, Paragraph [0053].

The "monocyclic non-aromatic heterocyclic group" is exemplified as an example of the "heterocyclic group."

[Definition of the <u>substituents</u> existing in the group described in the aforementioned (2)]

Page 10, Paragraph [0113].

The following explanations are described for the definition of the substituents of the functional group.

"In the present specification, when a certain functional group is defined as "which may be substituted," the definition means that the functional group may sometimes have one or more substituents at chemically substitutable positions, unless otherwise specifically mentioned. Kind of substituents, number of substituents, and the position of substituents existing in the functional groups are not particularly limited, and when two or more substituents exist, they may be the same or different. Examples of the substituent existing in the functional group include, for example, halogen atoms, oxo group, thioxo group, nitro group, nitroso group, cyano group, isocyano group, cyanato group, thiocyanato group, isocyanato group, isothiocyanato group, hydroxy group, sulfanyl group, carboxy group, sulfanylcarbonyl group, oxalo group, methooxalo group, thiocarboxy group, dithiocarboxy group, carbamoyl group, thiocarbamoyl group, sulfo group, sulfamoyl group, sulfino group, sulfinamoyl group, sulfeno group, sulfenamoyl group, phosphono group, hydroxyphosphonyl group, heterocyclic group, hydrocarbon-oxy hydrocarbon group, heterocyclic ring-oxy group, hydrocarbon-sulfanyl group, heterocyclic ring-sulfanyl group, acyl group, amino group, hydrazino group, hydrazono group, diazenyl group, ureido group, thioureido group, guanidino group, carbamoimidoyl group (amidino group), azido group, imino group, hydroxyamino group, hydroxyimino group, aminooxy group, diazo group, semicarbazino group, semicarbazono group, allophanyl group, hydantoyl group, phosphano group, phosphoroso group, phospho group, boryl group, silyl group, stannyl group, selanyl group, oxido group and the like."

(18) a halogen atom

According to the aforementioned (3), the "halogen atom" is thought to be an example of the substituent existing in the functional group.

(19) <u>an alkyl group which may be substituted with one or more</u> substituents

According to the aforementioned (5), the "alkyl group" is thought to be an example of the substituent existing in the functional group.

(20) a carboxy group (existing in the aforementioned "alkyl group")

According to the aforementioned (16), the "carboxy group" is thought to be an example of the substituent existing in the functional group.

(21) an alkoxy-carbonyl group (existing in the aforementioned "alkyl group")

According to the aforementioned (15), the "alkoxy-carbonyl group" is thought to be an example of the substituent existing in the functional group.

(22) a halogenated alkyl group

According to the aforementioned (6), the "halogenated alkyl group" is thought to be an example of the substituent existing in the functional group.

(23) a cyano group

According to the aforementioned (13), the "cyano group" is thought to be an example of the substituent existing in the functional group.

(24) an aryl group which may be substituted with one or more substituents

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Page 10, Paragraph [0113].

The "hydrocarbon group" is exemplified as an example of the substituent existing in the functional group.

Page 2, Paragraph [0028].

The "aryl group" is exemplified as an example of the "hydrocarbon group."

(25) a halogen atom (existing in the aforementioned "aryl group")

According to the aforementioned (3), the "alkoxy group" is thought to be an example of the substituent existing in the functional group.

(26) <u>a halogenated alkyl group (existing in the aforementioned "aryl group")</u>

According to the aforementioned (6), the "halogenated alkyl group" is thought to be an example of the substituent existing in the functional group.

(27) an alkoxy group (existing in the aforementioned "aryl group")

According to the aforementioned (7), the "alkoxy group" is thought to be an example of the substituent existing in the functional group.

(28) an alkyl-carbonyl group

Page 10, Paragraph [0113].

The "acyl group" is exemplified as an example of the substituent existing in the functional group.

Pages 7-8, Paragraph [0088].

The group represented by the formula $(\omega\text{-}1A)$ is exemplified as an example of the "acyl group."

Page 8, Paragraph [0089].

The "hydrocarbon-carbonyl group" is exemplified as an example of the group represented by the formula (ω -1A).

Page 2, Paragraph [0028].

The "aliphatic hydrocarbon group" is exemplified as an example of the "hydrocarbon group."

Pages 2-3, Paragraph [0029].

The "alkyl group" is exemplified as an example of the "aliphatic hydrocarbon group."

(29) an alkoxy-carbonyl group

According to the aforementioned (15), the "alkoxy-carbonyl group" is thought to be an example of the substituent existing in the functional group.

(30) <u>a monocyclic non-aromatic heterocyclic group which may be</u> substituted with one or more substituents

According to the aforementioned (17), the "monocyclic non-aromatic heterocyclic group" is thought to be an example of the substituent existing in the functional group.

(31) an alkyl group (existing in the aforementioned "monocyclic non-aromatic heterocyclic group")

According to the aforementioned (5), the "alkyl group" is thought to be an example of the substituent existing in the functional group.

(32) <u>an aryl group (existing in the aforementioned "monocyclic non-aromatic heterocyclic group")</u>

According to the aforementioned (24), the "aryl group" is thought to be an example of the substituent existing in the functional group.

(33) an aralkyl group

Page 10, Paragraph [0113].

The "hydrocarbon group" is exemplified as an example of the substituent existing in the functional group.

Page 2, Paragraph [0028].

The "aralkyl group" is exemplified as an example of the "hydrocarbon group."

(34) an aryl-carbonyl group

Page 10, Paragraph [0113].

The "acyl group" is exemplified as an example of the substituent existing in the functional group.

Pages 7-8, Paragraph [0088].

The group represented by the formula $(\omega$ -1A) is exemplified as an example of the "acyl group."

Page 8, Paragraph [0089].

The "hydrocarbon-carbonyl group" is exemplified as an example of the group represented by the formula $(\omega\text{-}1A)$.

Page 2, Paragraph [0028].

The "aryl group" is exemplified as an example of the "hydrocarbon group."

(35) a carbamoyl group which may be substituted with one or more substituents

Page 10, Paragraph [0113].

The "carbamoyl group" is exemplified as an example of the substituent existing in the functional group.

(36) an alkyl group (existing in the aforementioned "carbamoyl group")

According to the aforementioned (5), the "alkyl group" is thought to be an example of the substituent existing in the functional group.

(37) an aralkyl group (existing in the aforementioned "carbamoyl group")

According to the aforementioned (33), the "aralkyl group" is thought to be an example of the substituent existing in the functional group.

(38) a carboxy group

According to the aforementioned (16), the "carboxy group" is thought to be an example of the substituent existing in the functional group.

[Definition of Z]

Pages 1-2, Paragraph [0011], item (4).

"A benzene ring which may have one or more substituents" is defined as a group represented by "Z."

[Definition of the substituents existing in the aforementioned "benzene ring"]

Page 10, Paragraph [0113].

The following explanations are described for the definition of the substituents of the functional group.

"In the present specification, when a certain functional group is defined as "which may be substituted," the definition means that the functional group may sometimes have one or more substituents at chemically substitutable positions, unless otherwise specifically mentioned. Kind of substituents, number of substituents, and the position of substituents existing in the functional groups are not particularly limited, and when two or more substituents exist, they may be the same or different. Examples of the substituent existing in the functional group include, for example, halogen atoms, oxo group, thioxo group, nitro group, nitroso group, cyano group, isocyano group, cyanato group, thiocyanato group, isocyanato group, isothiocyanato group, hydroxy group, sulfanyl group, carboxy group, sulfanylcarbonyl group, oxalo group, methooxalo group, thiocarboxy group, dithiocarboxy group, carbamoyl group, thiocarbamoyl group, sulfo group, sulfamoyl group, sulfino group, sulfinamoyl group, sulfeno group, sulfenamovl group, phosphono group, hydroxyphosphonyl group, hydrocarbon group, heterocyclic group, hydrocarbon-oxy group, heterocyclic ring-oxy group, hydrocarbon-sulfanyl group, heterocyclic ring-sulfanyl group, acyl group, amino group, hydrazino group, hydrazono group, diazenyl group, ureido group, thioureido group, guanidino group, carbamoimidovl group (amidino group), azido group, imino group, hydroxyamino group, hydroxyimino group, aminooxy group, diazo group, semicarbazino group, semicarbazono group, allophanyl group, hydantoyl group, phosphano group, phosphoroso group, phospho group, boryl group, silyl group, stannyl group, selanyl group, oxido group and the like."

(39) a halogen atom

According to the aforementioned (3), the "alkoxy group" is thought to be an example of the substituent existing in the functional group.

(40) a nitro group

According to the aforementioned (4), the "nitro group" is thought to be an example of the substituent existing in the functional group.

(41) a cyano group

According to the aforementioned (13), the "cyano group" is thought to be an example of the substituent existing in the functional group.

(42) an alkoxy group

According to the aforementioned (7), the "alkoxy group" is thought to be an example of the substituent existing in the functional group.

(43) <u>an alkyl group which may be substituted with one or more</u> substituents

According to the aforementioned (5), the "alkyl group" is thought to be an example of the substituent existing in the functional group.

(44) <u>a hydroxy group (existing in the aforementioned "alkyl group")</u> Page 10, Paragraph [0113].

The "hydroxy group" is exemplified as an example of the substituent existing in the functional group.

(45) <u>an aralkyl-oxy-imino group (existing in the aforementioned "alkyl group")</u>

Page 10, Paragraph [0115].

The following explanations are described for the definition of the substituents existing in the functional group.

"The above substituents according to the aforementioned definition of "which may be substituted" may further be substituted with the aforementioned substituents at the chemically substitutable positions on the substituent. Kind of substituents, number of substituents, and positions of substituents are not particularly limited, and when the substituents are substituted with two or more substituents, they may be the same or different."

Page 10, Paragraph [0113].

The "imino group" is exemplified as an example of the substituent existing in the functional group.

Page 10, Paragraph [0113].

The "hydrocarbon-oxy group" is exemplified as an example of the substituent existing in the functional group.

Page 5, Paragraph [0059].

The "aralkyl-oxy group" is exemplified as an example of the "hydrocarbon-oxy group."

(46) an alkoxy-imino group (existing in the aforementioned "alkyl group") Page 10, Paragraph [0115].

The following explanations are described for the definition of the substituents existing in the functional group.

"The above substituents according to the aforementioned definition of "which may be substituted" may further be substituted with the aforementioned substituents at the chemically substitutable positions on the substituent. Kind of substituents, number of substituents, and positions of substituents are not particularly limited, and when the substituents are substituted with two or more substituents, they may be the same or different."

Page 10, Paragraph [0113].

The "imino group" is exemplified as an example of the substituent existing in the functional group.

Page 10, Paragraph [0113].

The "hydrocarbon-oxy group" is exemplified as an example of the substituent existing in the functional group.

Page 5, Paragraph [0059].

The "alkoxy group" is exemplified as an example of the "hydrocarbon-oxy group."

(47) an alkenyl group which may be substituted with one or more substituents

Page 10, Paragraph [0113].

The "hydrocarbon group" is exemplified as an example of the substituent existing in the functional group.

Page 2, Paragraph [0028].

The "aliphatic hydrocarbon group" is exemplified as an example of the "hydrocarbon group."

Pages 2-3, Paragraph [0029].

The "alkenyl group" is exemplified as an example of the "aliphatic hydrocarbon group."

(48) an aryl group (existing in the aforementioned "alkenyl group")

According to the aforementioned (24), the "aryl group" is thought to be an example of the substituent existing in the functional group.

(49) a cyano group (existing in the aforementioned "alkenyl group")

According to the aforementioned (13), the "cyano group" is thought to be an example of the substituent existing in the functional group.

(50) <u>an alkoxy-carbonyl group (existing in the aforementioned "alkenyl</u> group")

According to the aforementioned (15), the "alkoxy-carbonyl group" is thought to be an example of the substituent existing in the functional group.

(51) a carboxy group (existing in the aforementioned "alkenyl group")

According to the aforementioned (16), the "carboxy group" is thought to be an example of the substituent existing in the functional group.

(52) an alkynyl group which may be substituted with one or more substituents

Page 10, Paragraph [0113].

The "hydrocarbon group" is exemplified as an example of the substituent existing in the functional group.

Page 2, Paragraph [0028].

The "aliphatic hydrocarbon group" is exemplified as an example of the "hydrocarbon group."

Pages 2-3, Paragraph [0029].

The "alkynyl group" is exemplified as an example of the "aliphatic hydrocarbon group."

(53) an aryl group (existing in the aforementioned "alkynyl group")

According to the aforementioned (24), the "aryl group" is thought to be an example of the substituent existing in the functional group.

(54) <u>a tri(alkyl)silyl group (existing in the aforementioned "alkynyl</u> group")

Page 10, Paragraph [0115].

The following explanations are described for the definition of the substituents existing in the functional group.

"The above substituents according to the aforementioned definition of "which may be substituted" may further be substituted with the aforementioned substituents at the chemically substitutable positions on the substituent. Kind of substituents, number of substituents, and positions of substituents are not particularly limited, and when the substituents are substituted with two or more substituents, they may be the same or different."

Page 10, Paragraph [0113].

The "silyl group" is exemplified as an example of the substituent existing in the functional group.

Page 10, Paragraph [0113].

The "hydrocarbon group" is exemplified as an example of the substituent existing in the functional group.

Page 2, Paragraph [0028].

The "aliphatic hydrocarbon group" is exemplified as an example of the "hydrocarbon group."

Pages 2-3, Paragraph [0029].

The "alkyl group" is exemplified as an example of the "aliphatic hydrocarbon group."

(55) a halogenated alkyl group

According to the aforementioned (6), the "halogenated alkyl group" is thought to be an example of the substituent existing in the functional group.

(56) an aryl group which may be substituted with one or more substituents

According to the aforementioned (24), the "aryl group" is thought to be an example of the substituent existing in the functional group.

(57) a halogen atom (existing in the aforementioned "aryl group")

According to the aforementioned (3), the "halogen atom" is thought to be an example of the substituent existing in the functional group.

(58) a halogenated alkyl group (existing in the aforementioned "aryl group")

According to the aforementioned (6), the "halogenated alkyl group" is thought to be an example of the substituent existing in the functional group.

(59) an aralkyl group

According to the aforementioned (33), the "aralkyl group" is thought to be an example of the substituent existing in the functional group.

(60) a monocyclic or a fused polycyclic heteroaryl group which may be substituted with one or more alkyl groups

Page 10, Paragraph [0113].

The "heterocyclic group" is exemplified as an example of the substituent existing in the functional group.

Page 4, Paragraph [0053].

The "a monocyclic or a fused polycyclic heteroaryl group" is exemplified as an example of the "heterocyclic group."

(61) an alkyl group (existing in the aforementioned "monocyclic or fused polycyclic heteroaryl group")

According to the aforementioned (5), the "alkyl group" is thought to be an example of the substituent existing in the functional group.

(62) an alkyl-carbonyl group

According to the aforementioned (28), the "alkyl-carbonyl group" is thought to be an example of the substituent existing in the functional group.

(63) a monocyclic non-aromatic heterocyclic-carbonyl group which may be substituted with one or more aralkyl groups

Page 10, Paragraph [0113].

The "acyl group" is exemplified as an example of the substituent existing in the functional group.

Pages 7-8, Paragraph [0088].

The group represented by the formula $(\omega-1A)$ is exemplified as an example of the "acyl group."

Page 8, Paragraph [0089].

The "heterocyclic ring-carbonyl group" is exemplified as an example of the group represented by the formula $(\omega-1A)$.

Page 10, Paragraph [0113].

The "heterocyclic group" is exemplified as an example of the substituent existing in the functional group.

Page 4, Paragraph [0053].

The "monocyclic non-aromatic heterocyclic group" is exemplified as an example of the "heterocyclic group."

(64) an aralkyl group (existing in the aforementioned "monocyclic non-aromatic heterocyclic-carbonyl group")

According to the aforementioned (33), the "aralkyl group" is thought to be an example of the substituent existing in the functional group.

(65) a monocyclic heteroaryl-sulfonyl group

Page 10, Paragraph [0113].

The "acyl group" is exemplified as an example of the substituent existing in the functional group.

Pages 7-8, Paragraph [0088].

The group represented by the formula (ω -20A) is exemplified as an example of the "acyl group."

Page 9, Paragraph [0108].

The "heterocyclic ring-sulfonyl group" is exemplified as an example of the group represented by the formula $(\omega-20A)$.

Page 10, Paragraph [0113].

The "heterocyclic group" is exemplified as an example of the substituent existing in the functional group.

Page 4, Paragraph [0053].

The "monocyclic heteroaryl group" is exemplified as an example of the "heterocyclic group."

(66) a carboxy group

According to the aforementioned (16), the "carboxy group" is thought to be an example of the substituent existing in the functional group.

(67) an alkoxy-carbonyl group

According to the aforementioned (15), the "alkoxy-carbonyl group" is thought to be an example of the substituent existing in the functional group.

(68) a carbamoyl group which may be substituted with one or more substituents

According to the aforementioned (35), the "carbamoyl group" is thought to be an example of the substituent existing in the functional group.

(69) an aryl group (existing in the aforementioned "carbamoyl group")

According to the aforementioned (24), the "aryl group" is thought to be an example of the substituent existing in the functional group.

(70) an halogenated alkyl group (existing in the aforementioned "aryl group")

According to the aforementioned (6), the "halogenated alkyl group" is thought to be an example of the substituent existing in the functional group.

(71) an alkyl group (existing in the aforementioned "carbamoyl group")

According to the aforementioned (5), the "alkyl group" is thought to be an example of the substituent existing in the functional group.

(72) <u>a sulfamoyl group which may be substituted with one or more</u> substituents

Page 10, Paragraph [0113].

The "carbamoyl group" is exemplified as an example of the substituent existing in the functional group.

(73) an aryl group (existing in the aforementioned "sulfamoyl group")

According to the aforementioned (24), the "aryl group" is thought to be an example of the substituent existing in the functional group.

(74) an halogenated alkyl group (existing in the aforementioned "aryl group")

According to the aforementioned (6), the "halogenated alkyl group" is thought to be an example of the substituent existing in the functional group.

(75) an alkyl group (existing in the aforementioned "sulfamoyl group")

According to the aforementioned (5), the "alkyl group" is thought to be an example of the substituent existing in the functional group.

(76) an amino group which may be substituted with one or more substituents

Page 10, Paragraph [0113].

The "amino group" is exemplified as an example of the substituent existing in the functional group.

(77) an alkyl group (existing in the aforementioned "amino group")

According to the aforementioned (5), the "alkyl group" is thought to be an example of the substituent existing in the functional group.

(78) an alkyl-carbonyl group (existing in the aforementioned "amino group")

According to the aforementioned (28), the "alkyl-carbonyl group" is thought to be an example of the substituent existing in the functional group.

(79) <u>an aryl-carbonyl group (existing in the aforementioned "amino group")</u>

According to the aforementioned (34), the "aryl-carbonyl group" is thought to be an example of the substituent existing in the functional group.

(80) an alkyl-sulfonyl group (existing in the aforementioned "amino group")

Page 10, Paragraph [0113].

The "acyl group" is exemplified as an example of the substituent existing in the functional group.

Pages 7-8, Paragraph [0088].

The group represented by the formula (ω -20A) is exemplified as an example of the "acyl group."

Page 9, Paragraph [0108].

The "hydrocarbon-sulfonyl group" is exemplified as an example of the group represented by the formula (ω -20A).

Page 2, Paragraph [0028].

The "aliphatic hydrocarbon group" is exemplified as an example of the "hydrocarbon group."

Pages 2-3, Paragraph [0029].

The "alkyl group" is exemplified as an example of the "aliphatic hydrocarbon group."

(81) an aryl-sulfonyl group (existing in the aforementioned "amino group")

Page 10, Paragraph [0113].

The "acyl group" is exemplified as an example of the substituent existing in the functional group.

Pages 7-8, Paragraph [0088].

The group represented by the formula (ω -20A) is exemplified as an example of the "acyl group."

Page 9, Paragraph [0108].

The "hydrocarbon-sulfonyl group" is exemplified as an example of the group represented by the formula (ω -20A).

Page 2, Paragraph [0028].

The "aryl group" is exemplified as an example of the "hydrocarbon group."

(82) an ureido group which may be substituted with one or more aryl groups

Page 10, Paragraph [0113].

The "ureido group" is exemplified as an example of the substituent existing in the functional group.

(83) an aryl group (existing in the aforementioned "ureido group")

According to the aforementioned (24), the "aryl group" is thought to be an example of the substituent existing in the functional group.

(84) a thioureido group which may be substituted with one or more aryl groups

Page 10, Paragraph [0113].

The "thioureido group" is exemplified as an example of the substituent existing in the functional group.

(85) an aryl group (existing in the aforementioned "thioureido group")

According to the aforementioned (24), the "aryl group" is thought to be an example of the substituent existing in the functional group.

(86) a diazenyl group which may be substituted with one or more aryl groups

Page 10, Paragraph [0113].

The "diazenyl group" is exemplified as an example of the substituent existing in the functional group.

(87) an aryl group (existing in the aforementioned "diazenyl group")

According to the aforementioned (24), the "aryl group" is thought to be an example of the substituent existing in the functional group.

(88) a nitro group (existing in the aforementioned "aryl group")

According to the aforementioned (4), the "nitro group" is thought to be an example of the substituent existing in the functional group.

(89) <u>a monocyclic heteroaryl-sulfamoyl group (existing in the aforementioned "aryl group")</u>

Page 10, Paragraph [0115].

The following explanations are described for the definition of the substituents existing in the functional group.

"The above substituents according to the aforementioned definition of "which may be substituted" may further be substituted with the aforementioned substituents at the chemically substitutable positions on the substituent. Kind of substituents, number of substituents, and positions of substituents are not particularly limited, and when the

substituents are substituted with two or more substituents, they may be the same or different."

Page 10, Paragraph [0113].

The "sulfamoyl group" is exemplified as an example of the substituent existing in the functional group.

Page 10, Paragraph [0113].

The "heterocyclic group" is exemplified as an example of the substituent existing in the functional group.

Page 4, Paragraph [0053].

The "monocyclic heteroaryl group" is exemplified as an example of the "heterocyclic group."

(90) a hydroxy group

According to the aforementioned (44), the "hydroxy group" is thought to be an example of the substituent existing in the functional group.

Claim 32

[Method claim]

Page 2, Paragraph [0019].

Claim 33

[Method claim]

Page 2, Paragraph [0019].

Claim 34

[Method claim]

Pages 123-124, Test Examples 1, 2, 5 and 6.

Claim 35

[Definition of the <u>substituents</u> of E]

(1) a phenyl-oxy group

Page 3, Paragraph [0045].

The "phenyl group" is exemplified as an example of the "aryl group."

(2) a naphthyl-oxy group

Page 3, Paragraph [0045].

The "naphthyl group" is exemplified as an example of the "aryl group."

(3) a 1-pyrrolidinyl group

Page 5, Paragraph [0058].

The "1-pyrrolidinyl group" is exemplified as an example of the "monocyclic non-aromatic heterocyclic group."

(4) a piperidino group

Page 5, Paragraph [0058].

The "piperidino group" is exemplified as an example of the "monocyclic non-aromatic heterocyclic group."

(5) a morpholino group

Page 5, Paragraph [0058].

The "morpholino group" is exemplified as an example of the "monocyclic non-aromatic heterocyclic group."

(6) a phenyl group

Page 3, Paragraph [0045].

The "phenyl group" is exemplified as an example of the "aryl group."

(7) a 1-piperazinyl group

Page 5, Paragraph [0058].

The "1-piperazinyl group" is exemplified as an example of the "monocyclic non-aromatic heterocyclic group."

(8) a benzyl group

Page 4, Paragraph [0048].

The "benzyl group" is exemplified as an example of the "aralkyl group."

(9) a phenyl-carbonyl group

Page 3, Paragraph [0045].

The "phenyl group" is exemplified as an example of the "aryl group."

(10) a phenyl-alkyl group

Page 4, Paragraph [0048].

The following explanations are described for the definition of the aralkyl group.

"Examples of the aralkyl group include the groups in which one hydrogen atom of the alkyl group is substituted with an aryl group,"

Claim 36

[Definition of E]

Pages 23-24, Paragraphs [0242], [0246], [0256] and [0258].

Claim 37

[Definition of the <u>substituents</u> of Z]

(1) a benzyl-oxy-imino group

Page 4, Paragraph [0048].

The "benzyl group" is exemplified as an example of the "aralkyl group."

(2) a phenyl group

Page 3, Paragraph [0045].

The "phenyl group" is exemplified as an example of the "aryl group."

(3) a phenyl-alkyl group

Page 4, Paragraph [0048].

The following explanations are described for the definition of the aralkyl group.

"Examples of the aralkyl group include the groups in which one hydrogen atom of the alkyl group is substituted with an aryl group,"

(4) a 1-pyrrolyl group, a 2-pyrrolyl group, and a 3-pyrrolyl group

Page 4, Paragraph [0054].

These groups are exemplified as an example of the "monocyclic heteroaryl group."

(5) a 2-thienyl group, and a 3-thienyl group

Page 4, Paragraph [0054].

These groups are exemplified as an example of the "monocyclic heteroaryl group."

(6) a 2-thiazolyl group, a 4-thiazolyl group, and a 5-thiazolyl group

Page 4, Paragraph [0054].

These groups are exemplified as an example of the "monocyclic heteroaryl group."

(7) a 2-pyridyl group, a 3-pyridyl group, and a 4-pyridyl group

Page 4, Paragraph [0054].

These groups are exemplified as an example of the "monocyclic heteroaryl group."

(8) an imidazo[1,2-a]pyridin-2-yl group

Pages 21-22, Paragraph [0235].

(9) a piperidino-carbonyl group

Page 5, Paragraph [0058].

The "piperidino group" is exemplified as an example of the "monocyclic non-aromatic heterocyclic group."

(10) <u>a 1-pyrrolyl-sulfonyl group</u>, <u>a 2-pyrrolyl-sulfonyl group</u>, <u>and a 3-pyrrolyl-sulfonyl group</u>

Page 4, Paragraph [0054].

The pyrrolyl group, 2-pyrrolyl group and 3-pyrrolyl group are exemplified as an example of the "monocyclic heteroaryl group."

(11) a phenyl-carbonyl group

Page 3, Paragraph [0045].

The "phenyl group" is exemplified as an example of the "aryl group."

(12) a phenyl-sulfonyl group

Page 3, Paragraph [0045].

The "phenyl group" is exemplified as an example of the "aryl group."

(13) <u>a 2-pyridyl-sulfamoyl group</u>, a 3-pyridyl-sulfamoyl group, and a 4-pyridyl-sulfamoyl group

Page 4, Paragraph [0054].

The -pyridyl group, 3-pyridyl group, and 4-pyridyl group are exemplified as an example of the "monocyclic heteroaryl group."

Claim 38

[Definition of the partial formulas (Iz-1) and (Iz-2)]

Pages 21-22, Paragraph [0235].

[Definition of R^z]
Pages 21-22, Paragraph [0235].

R^z is defined as a substituent of Z.

Claim 40

[Definition of R^z]
Pages 21-22, Paragraph [0235].

Formal Matters

Applicants note with appreciation that the Office Action acknowledges the Claim of Priority under 35 U.S.C. § 119 and confirms that all copies of the certified copies of the priority document have been received by the Office.

Applicants also note with appreciation that the Action includes signed and initialed copies of the Forms PTO-1449 submitted in the Information Disclosure Statements of July 28, 2006 and March 7, 2006, indicating that the Examiner has taken the submitted material under consideration.

Status of Claims

Applicants thank the Examiner for a telephone conversation on February 8, 2008 with Dr. Thomas Weber. During the telephone conversation, it was clarified that the listing of claims 13-16, 18-23, 24-27, and 30-31 as being withdrawn was an inadvertent typographical error by the Examiner and that claims 12-17, 25-27, and 30-31 -- as listed on the summary sheet of the Office Action -- are currently withdrawn. As a result and upon entry of the foregoing amendments to the claims, claims 1, 28, and 29 are currently under examination, claims 30-31 are withdrawn, and claims 1, 28-41 are pending.

Claim Objections

The objection to claim19 is most in view of the cancellation of the claim.

Claim Rejections under 35 U.S.C. 112, second paragraph

The Office Action rejects claims 1, 18-24, and 28-29 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to clearly point out and distinctly claim the subject matter. As for these claims, the Action asserts that the term "and/or" in claim 1 renders the claim unclear.

In view of the foregoing amendments to the claims, Applicants submit that the claims have been amended to render them in better conformance with 35 U.S.C. § 112, second paragraph. Withdrawal of the rejection is respectfully requested.

In view of the cancellation of claim 19, the rejection of this claim under § 112 is moot.

Claim Rejections under 35 U.S.C. 112, first paragraph

The Office Action rejects claims 1, 18-24, and 28-29 under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement. The Examiner asserts that the specification lacks support to demonstrate how the treatment using a compound represented in claim 21 can have prophylactic/curative for any and all cancers.

Applicants respectfully traverse this rejection and submit that Examples 1 to 6 in the specification clearly demonstrate that Compound No. 4 has inhibitory activity against proliferation of a variety of tumor cells as well as inhibitory activity against metastasis of tumor cells and anticancer activity. In the same manner, compounds according to formula (I) that are structurally similar to Compound No. 4 were also shown to have the inhibitory activity against proliferation of tumor cells. Accordingly, one of ordinary skill in the art would readily be able to recognize that the above compounds are useful for treatment of tumors or cancers. Furthermore, Applicants submit that one of ordinary skill in the art would also expect that compounds that fall within the scope of present claim 1 to exhibit inhibitory activity against proliferation of tumor cells and conclude the beneficial use for treatment of cancer. In comparison, Applicants direct the Examiner's attention to U.S. Patent No. 6,492,425 to Callahan et al. (hereinafter "Callahan", raised by the Examiner in the obviousness rejection), where Callahan's allowed claims are only supported by a number of eight (8) compounds specifically disclosed in the specification. In addition, Applicants submit that the skilled artisan would expect that a prophylactic treatment is possible and can be conducted by inhibition of proliferation or metastasis of tumor cells at an early stage in order to prevent the generation of a primary cancer or metastatic cancer.

The Office Action further rejects claims 1, 18-24, and 28-29 under 35 U.S.C. § 112, first paragraph, for allegedly failing to enable the phrase "and a hydrate thereof and a solvate thereof."

Applicants respectfully traverse this rejection. Initially, Applicants submit that claim 1 has been amended to further clarify that the scope of compounds according to formula (I) includes hydrates or solvates and not a hybrid complex of a hydrate and a solvate. Applicants submit that a hydrate or a solvate can be prepared by various processes well known in the art as described in paragraph [0273] of the published application. Furthermore, the skilled artisan would know that a hydrate or a solvate of the claimed compound substantially has the same pharmacological activity as the free compound. In contrast, Callahan has no specific support in the specification for the hydrates or solvates as recited in the allowed claims. Apparently, according to the specification of Callahan, hydrates or solvates of free compounds are well known in the art and therefore, the claimed invention does not necessitate specific examples of any hydrates or any solvates.

Nonstatutory Obviousness-Type Double-Patenting

The Office Action provisionally rejects claims 1, 18-24, and 28-29 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of copending U.S. Patent Application No. 10/546,407 and further in view of Mukhopadhyay et al., Oncogene, vol. 11, no. 5, 1995, pp. 999-1003 (abstract only) (hereinafter "Mukhopadhyay").

Applicants respectfully request that this <u>provisional</u> obviousness-type double patenting rejection be held in abeyance until the Examiner has indicated allowable subject

matter in the present application and allowable subject matter has also been indicated in the co-pending application. Without knowing which claims in the present application and which claims in the co-pending application will be allowed, Applicants are unable to determine if the filing of a terminal disclaimer is necessary.

Claim Rejections under 35 U.S.C. § 103(a)

The Office Action rejects claims 1, 18-24, and 28-29 under 35 U.S.C. § 103(a) as being unpatentable over Callahan in view of Mukhopadhyay. More specifically, the Action asserts that Callahan teaches methods of treatment of diseases associated with NF-κB activation. The Action relies on Mukhopadhyay for disclosure of NF-κB activation in connection with non-small cell lung carcinoma. Although, Callahan does not identify compound No. 4 as elected in response to the previous Restriction Requirement, the Action assert that compound No. 4 would be obvious to someone of skill in the pertinent art.

Applicants respectfully traverse this rejection. As the Examiner is well aware, for a *primae facie* obviousness rejection, each and every feature of the rejected claim has to be disclosed or suggested in the cited art. Applicants respectfully submit that neither Callahan nor Mukhopadhyay disclose any compound that fall within the scope of the present claims.

The present claims recite that a compound of formula (I) comprises "at least one trifluoromethyl group." The Examiner concedes that Callahan fails to disclose such

moiety but asserts that it would have been obvious to the skilled artisan to modify Callahan to arrive at the compounds of the present claims. Applicants respectfully request that the Examiner substantiate this assertion especially in view of the fact that:

- (a) none of the exemplified compounds in Callahan has a corresponding E ring that is either 2,5- or 3,5-disubstituted as recited in present claim 1;
- (b) none of the compounds in Callahan permits a trifluoromethyl group substituted on the corresponding E ring;
- (c) even assuming, *arguendo*, that a combination with Mukhopadhyay is proper, the combined references fail to show how any compound of Callahan would be useful as a prophylactic or therapeutic treatment of cancerous diseases or generation of cancer.

As for point (b), Applicants further submit that although Callahan discloses trifluoromethyl groups available for Callahan's A ring (corresponding to ring Z in general formula (I)), Callahan disfavors such substitution for its B ring (corresponding to Applicants' moiety E). In support for this statement, Applicants direct the Examiner's attention to Callahan, column 4, lines 42-43, "Any C₁₋₆ alkyl group may be optionally substituted independently by one or two halogens, . . ." (emphasis added).

In view of the forgoing, Applicants submit that Callahan in view of Mukhopadhyay fails to render the present claims obvious. Withdrawal is respectfully requested.

CONCLUSION

For the reasons discussed above, it is respectfully submitted that the rejections be withdrawn. Favorable consideration with early allowance of all of the pending claims is most earnestly requested.

If there are any comments or questions, the undersigned may be contacted at the below-listed telephone number.

Respectfully submitted, Susumu MUTO et al.

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